REMARKS/ARGUMENTS

Interview Summary

Applicants thank Examiner David Kruse for the courtesy of the telephonic interview on December 22, 2009, where amendments to claims 71 and 79 were discussed. Applicants' representative Yifan Mao and the Examiner have agreed on amending these claims by specifying the program and parameters used to determine the percent identity ("using BLASTP program using as defaults a wordlength (W) of 3, an expectation (E) of 10, and the BLOSUM62 scoring matrix") and by adding the claim element: "polypeptide that regulates transcription". The obviousness rejection and the breath of the claims from the recent Office action have also been discussed during the interview. Applicants held that the claims are directed to transgenic plants possessing the trait of conferring greater tolerance to water deprivation relative to controls, which is not inherent and unobvious over the plants disclosed in the prior art. Applicants stated that claim 71 recites not only the 60% overall amino acid identity to SEQ ID NO: 4, but also the limitations directed to the first, second and third domains (claim 71).

Amendments to the claims.

Claims 71, 76 and 79 have been currently amended. Claims 72-75 and 77-78 were previously presented. Claims 80-82 are new claims added by the amendment. After this amendment, claim 71-82 will remain in this application.

Support for "wherein the percent identity is determined using BLASTP program using as defaults a wordlength (W) of 3, an expectation (E) of 10, and the BLOSUM62 scoring matrix" in claim 71 is found at page 85, lines 23-25.

Support for "85%" is found at "More closely related transcription factors can share at least about 79% or about 90% or about 95% or about 98% or more sequence identity with the listed sequences, or with the listed sequences but excluding or outside a known consensus sequence or consensus DNA-binding site, or with the listed sequences excluding one or all conserved domains. Factors that are most closely related to the listed sequences share, e.g., at

least about 85%, about 90% or about 95% or more % sequence identity to the listed sequences, or to the listed sequences but excluding or outside a known consensus sequence or consensus DNA-binding site or outside one or all conserved domain" (lines 2-14 at page 55).

No new matter is added by this amendment. Entry of this amendment is respectfully requested.

Response to specific items within the Office action.

Item 3, 4, and 5. Rejection under 35 USC 112, second paragraph and first paragraph,

Claims 71-73 and 76-79 have been rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. This rejection has been in part avoided by the present amendment and in part respectfully traversed for the reasons set forth below. The specific elements in the Office action are presented in boldface.

The claimed genus is to G922, SEQ ID NO: 4 and sequences that are closely related to G922. The pending claims 71-78 recite a functional limitation, i.e., conferring greater tolerance to water deprivation as compared to a control plant, and also require a predictable structure of at least 60% amino acid sequence identity to G922, SEQ ID NO: 4, and 68% amino acid sequence identity to the 1st SCR domain, 74% amino acid sequence identity to the 2nd SCR domain, and 60% amino acid sequence identity to the 3rd SCR domain. Claims 79-81 are directed to transgenic plants comprising recombinant polypeptides that have very high structural similarity, i.e., at least 85%, 95% and 100% to G922 (SEQ ID NO: 4).

> **At claim 71 (currently amended),**
> **lines 3-4, the limitation "comprises a first conserved domain that is at least 65% identical to amino acids 134-199 of SEQ 10 NO: 4" is New Matter. Applicants' assertion that parent application 10/675,852, paragraph 0081, supports this limitation is not found to be persuasive because said parent application make no reference to G922 (SEQ NO: 4), nor does it make reference to a "first conserved domain". The instant specification does not provide adequate written description support for all of the limitations in instant claim 71 (the last paragraph at page 1 of the Office action).**

Written description support for the newly added claim element "68% sequence identity", can be found in Table 1 on page 36, in the rows "212…G3810…1st SCR: 106-171…316-

513…[% ID in conserved domain: %ID to G922] 68%, and "214…G3811…1st SCR: 103-168…361-558…[% ID in conserved domain: %ID to G922] 68%".

The Office's alignment shows a percent identity of 57.2% not 62.8%. The instant claims do not set forth what method percent identity is to be used. i.e. there is no reference in claim 71 to an Accelrys based method. The provided alignments between G922 and G3811 are not based on the complete amino acid sequence of SEQ ID NO: 4, only amino acids 37-482 (the third paragraph at page 3 of the Office action).

In response, Applicants have provided the alignment by BLASTP program (please see Exhibit A of the previous response submitted on 24 August 2009), which shows that G3811 and G922 share 61% sequence identity. Applicants have also amended claim 71 to specify the method of determining the percent identity as "the BLASTP program using as defaults a wordlength (W) of 3, an expectation (E) of 10, and the BLOSUM62 scoring matrix", which is supported by the specification at page 85, lines 23-25. The specification has clearly taught using BLAST to determine the percent identity between two proteins, for example, page 55 lines 29-30:"[o]ther alignment algorithms or programs may be used, including FASTA, BLAST, or ENTREZ, FASTA and BLAST, and which may be used to calculate percent similarity". As such, G3811 is encompassed by the claims.

Applicants provide no evidence of what "conserved domain" is required, to provide the specific function of the claimed genus (confers to the transgenic plant greater tolerance to water deprivation) The domains described do not appear to describe a specific function.

Conserved domains are known to be correlated with transcription factor function in general (page 20, lines 27-28), conserved domain database at the National Center for Biotechnology Information (presently at www.ncbi.nlm.nih.gov/Structure/cdd/cdd_help.shtml#CDModelIllustration), regarding the relationship between the conserved domain and the function of a protein: "[d]omains can be thought of as distinct functional and/or structural units of a protein. These two classifications coincide rather often, as a matter of fact, and what is found as an independently folding unit of a polypeptide chain also carries specific function. Domains are often identified as recurring

(sequence or structure) units, which may exist in various contexts. …In molecular evolution such domains may have been utilized as building blocks, and may have been recombined in different arrangements to modulate protein function. We define conserved domains as recurring units in molecular evolution, the extents of which can be determined by sequence and structure analysis".

Please also see Doerks (2002) *Genome Res.* 12: 47–56: "The independent evolutionary histories of domains found within the same protein lead to an assumption that the domain is the fundamental unit of protein structure and function" (page 47, column 1), and "Conserved protein domains are most useful when they can be used to make predictions of likely function" (page 49, column 2), and "On the basis of reports in the literature and/or co-occurrence with previously identified domains, some functional features can be predicted for 78.6% of our newly identified set of 28 domain families. This represents an increase in the state of functional prediction for ~700 proteins (i.e., the total number of distinct proteins that are covered by novel domains with a putative function" (page 53, column 1). Thus, it is well established that evolutionarily conserved domains may be used to characterize both structure and function.

It is well known in the art that protein functions can be classified using phylogenetic analysis, for example, with multiple alignments and/or phylogenetic trees, which allows one to identify structural and functional boundaries, thus establishing a basis for accurate predictions based on a specific, experimentally determined level of relatedness. The art also recognizes that functional predictions can be greatly improved by focusing on how the genes became similar in sequence (i.e., by evolutionary processes) rather than on the sequence similarity itself (page 163, col. 1, Eisen, 1998, attached). In fact, many specific examples exist in which gene function has been shown to correlate well with gene phylogeny (page 165, col. 3, ¶2, Eisen, 1998). Figure 20 of the specification shows that a number of G922 clade members are phylogenetically related, and the specification determines the boundaries of the G922 functional clade.

The instant specification taught that the claimed genus belongs to the SCR (SCARECROW) gene family, which is part of GRAS gene family of transcription factors (lines 14-26 at page 29), where the conserved domains (SCR domains) are art-recognized as important for the activity of this family of transcription factors: "proteins in the GRAS family are

transcription factors that seem to be involved in development and other processes." (the GRAS domain of the NCBI conserved domain database, attached). "GRAS gene family members "share a variable amino-terminus and a highly conserved carboxyl-terminus that contains five recognisable motifs (LHRI, VHIID, LHRII, PFYRE and SAW motifs)" (please see the sequence alignments in Figure 1 of Pysh et al., 1999, provided by the Examiner). Pysh also taught that the LHRI and LHRII are involved in protein multimerization " the presence of leucine heptad repeats in the GRAS proteins suggests that these gene products may function as multimers" (Pysh et al., 1999, page 112, 2nd column, second paragraph), and that the VHIID region of the different SCR proteins bear striking similarity to each other, the P-N-H-D-Q-L residues are absolutely conserved (*Id,* page 112, 2nd column, third paragraph); The sequences within the PFYRE domain are largely co-linear and portions of this region show a high degree of sequence similarity among all members of the family. Pysh summarized that "the GRAS gene products are characterized by a variable N-terminal region and a highly conserved c-terminal region. Importantly, the order of these motifs within each protein is the same. While the functions of the VHIID, PFYRE and SAW motifs are currently unknown, the absolute conservation of the residues in the VHIID and SAW motifs indicates that these residues are required for the activity of the GRAS gene products." (*Id*, page 113, 2nd paragraph). Pysh did not test any of the SCR genes in a transgenic setting, in contrast, Applicants have introduced a subgroup of SCR genes with distinct structural features as claimed, including G922, G3810, and G3188, into plants and vigorously tested and showed that they all conferred greater tolerance to water deprivation compared to controls.

Applicants have provided in Table 1 the identifying structural elements: the three conserved SCR domains that are homologous to that of SEQ ID NO: 4 through sequence alignments as shown in Figure 19A-19R, and also described a fourth "ser/pro-rich domain that is unique to the G922 clade (lines 11-12 at page 10). Applicants have provided three representative variants: G3811, G3810 and G922, which are derived from different plant species, which have the sequence identity of 61%, 65% and 100% to SEQ ID NO: 4, and have the function of conferring greater water deprivation tolerance to transgenic plants when over-expressed relative to controls. G3811 and G3810 are the only orthologs of G922 that have been tested to date.

Applicants have also disclosed the conserved structural elements, i.e., the three conserved SCR domains corresponding to amino acids 134-199, 332-401 and 405-478 of SEQ ID NO: 4, which are always present in the sequences that have functioned by conferring water deprivation tolerance. Since these sequences are derived from diverse plant species, (both *Arabidopsis* and soy), they represent a practical sampling of a large number of sequence species. Applicants believe that in view of the significant structure/function relationships disclosed in the cited references and conserved domain disclosed in the specification in combination with the disclosed working examples, one of ordinary skill in the art would recognized that the three conserved domains with high homology and the overall homology to SEQ ID NO: 4 are correlated with the function of conferring greater tolerance to water deprivation.

Those skilled in the art would recognize that members of the claimed genus would have properties similar to those of SEQ ID NO: 4 because of the high degree of structural similarity. It is noted that Applicants are not required to reason why the invention works, rather, Applicants can show "possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including a description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it"). As stated above, Applicants have fully described the claimed genus of sequences that have at least 60% amino acid sequence identity to SEQ ID NO: 4, and a first conserved domain that is at least 68% identical to amino acids 134-199 of SEQ ID NO: 4, a second conserved domain that is at least 74% identical to amino acids 332-401 of SEQ ID NO: 4, and a

third conserved domain that is at least 60% identical to amino acids 405-478 of SEQ ID NO: 4; said sequences can confer greater tolerance to water deprivation to a plant relative to controls.

Please also see Example 11B of the Written Description Training Materials, rev. March 25, 2008, which teaches that when there is an "Art-Recognized Structure-Function Correlation Present", where the written description requirement for a claim to 85% identity to a specific protein is met given a disclosure of the "reduction to practice of only a single species that encodes SEQ ID NO: 2 and has activity Y, i.e., SEQ ID NO: 1. There are no other drawings or structural formulas disclosed of a nucleic acid that encodes either (i) SEQ ID NO: 2 or (ii) a polypeptide with 85% sequence identity to SEQ ID NO: 2 wherein the polypeptide also has activity Y....Nonetheless, the specification identifies two domains responsible for activity Y, i.e., a binding domain and catalytic domain. The specification also predicts that conservative mutations in these domains will result in a protein having activity Y. Although all conservative amino acid substitutions in these domains will not necessarily result in a protein having activity Y, those of ordinary skill in the art would expect that many of these conservative substitutions would result in a protein having the required activity."...

Please compare Example 11B with the instant disclosure, which identifies the structure of SEQ ID NO: 4. This sequence is readily identifiable as an SCR-related transcription factor protein, as indicated in the Pysh citation and in the specification on page 188, lines 7-12. G922 possesses at least four distinct domains, disclosed as indicated above. Unlike Example 11B, the specification discloses phylogenetically related sequences: in the Table on pages 36-37 and on page 119, lines 13-16. The instant specification also provides an extensive discussion of conservative substitutions, silent mutations, etc., beginning on page 64 at line 4 through page 66, line 13.

The data disclosed and submitted in the declarations of Drs. Reuber and Ratcliffe show a definitive correlation between the claimed domains and function, thus establishing a structure-function relationship. And, as Example 11B of the Training Materials teaches, "amino acid substitutions outside of the two identified functional domains *are unlikely to greatly affect activity Y. Thus, a correlation exists between the function of the claimed protein and the structure of the disclosed binding and catalytic domains*" (*emphasis* added). Furthermore, non-

functional species would be excluded by the language of the claims. All claim limitations, including functional language, are entitled to patentable weight.

Table 1, at pages 35 and 36 of the instant specification identifies several "G922 orthologous", Applicants evidence only demonstrates that two of the five orthologous produce the claimed phenotype.

The sequence species that were shown to function in plants are derived from diverse plant species, *Arabidopsis* and soy, representing the orders of Capparales and Fabales, respectively. Functional species that derive from widely diverse species have been held by the UPSTO to embody a representative number of species": a " "representative number of species" requires that the species which are expressly described be representative of the entire genus. Thus, when there is substantial variation within the genus, it may require a description of the various species which reflect the variation within the genus. For example, a broadly drawn claim to a specific gene from ruminant mammals may require a representative species from cattle, buffalo, bison, goat, deer, antelope, camel, giraffe and llama" (Request for Comments on Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 1 "Written Description" Requirement", 1998. Docket No. 980605148-8148-01). Note that the ruminants are members of the same order, Artiodactyla, whereas soy and *Arabidopsis* are members of different orders, and are thus even more evolutionarily distant than the species provided in the USPTO example.

Applicants note that even the broadest claim of the present invention is limited to sequences that have at least 60% sequence identity to the whole protein of G922, and the three conserved domain that are highly similar to those of G922, SEQ ID NO: 4. Out of the five G922 orthologs disclosed in Table 1, only G3810, G3811, and G3824 share overall percent identity of greater than 60% by BLASTp using the parameters described in this amendment. The other three, namely, G3813, and G3814, G3827, sharing only 52% and 41%, and 56% amino acid sequence identity to SEQ ID NO: 4, are not encompassed by the claims (please see the sequence alignment in Exhibit A), therefore, Applicants are not required to demonstrate their function. G3824 shares 69% sequence identity to SEQ ID NO: 4, but its function has not been tested in transgenic plants. It is noted that Applicants are not required to exemplify each and every

claimed embodiment of his or her invention. Rather, "if a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then adequate written description requirement is met" (*In re Alton*, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996)). The three other disclosed functional polypeptide sequences, G922, G3810 and G3811, which are derived from very diverse plant species, including soy and *Arabidopsis,* represent a considerably large number of plant sequence species that have the similar structure and function as that of G922. Federal circuit has held that a "claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention…" *Falkner b. Inglis*, 448 f. 3d 1357, 1366, 79 U.S.P.Q. 2d 1001 (Fed. Cir. 2006), quoting from *LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.*, 424 f. 3d 1336, 1345 (Fed. Cir. 2005). In view of the disclosure of the specification, one of ordinary skill in the art would clearly recognize that Applicants were in possession of the claimed invention at the time of filing.

Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, for lack of written description, be withdrawn.

Item 6. Rejection under 35 USC 112, first paragraph, enablement

Claims 71-73 and 76-79 have been rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the enablement requirement. This rejection has been in part avoided by the present amendment and in part respectfully traversed for the reasons set forth below. The specific elements in the Office action are presented in boldface.

Applicants' statement that "the polypeptides in the claimed invention are not limited to the transcription factors or peptides that can regulate transcription" is unclear because the species

Applicants' assert as being enabling are transcription factors that can regulate transcription factors.

Applicants respectfully disagree with the Examiner's assessment. However, in the interest of advancing the prosecution, Applicants have amended the claim and limited the claims to direct to the polypeptides that regulate transcription when expressed in plants.

Applicants have only taught how to make and use two species at the extremes of the claimed genus, said claimed genus comprising a vast number of species having the claimed "domains" but not having the claimed function.

In response, Applicants note that the claimed sequences not only have high sequence homology to G922, but also have all three conserved domains. Applicants have provided three representative variants: G3811, G3810 and G922, which have the sequence identity of 61%, 65% and 100% to SEQ ID NO: 4, and have the function of conferring greater water deprivation tolerance to transgenic plants relative to controls when over-expressed. It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. *In re Angstadt*, 537 f. 2d 498, 502-03, 190 USPQ 214, 218 (CCPA 1976). However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill in the art how to make and how to use the invention as broadly as it is claimed. This means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility (*In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991)). The disclosed polypeptide sequences (working examples) having the described structure and function are derived from very diverse species, including soy and Arabidopsis and they represent a considerably large number of plant sequence species. There is also significant disclosure of methods for making and screening sequences that are at least 60% identical to SEQ ID NO: 4, and have a first conserved domain that is at least 68% identical to amino acids 134-199 of SEQ ID NO: 4, a second conserved domain that is at least 74% identical to amino 332-401 of SEQ ID NO: 4, and a third conserved domain that is at least 60% identical to amino 405-478 of SEQ ID NO: 4, expressing the polypeptide in the transgenic plant, and testing for the ability of conferring greater tolerance to water deprivation as compared to a control plant (please see Examples I-V and VIII). Applicants have also disclosed the conserved structural elements, i.e., the three

conserved SCR domains corresponding to amino acids 134-199, 332-401 and 405-478 of SEQ ID NO: 4, which are always present in the sequences that have functioned by conferring water deprivation tolerance. Further, the related art has teachings regarding the conserved residues that are critical for the activity of the protein, for example, Pysh et al.(1999) has disclosed the five recognizable motifs present in the highly conserved carboxyl-terminus and the absolutely conserved residues in these motifs among the GRAS gene family members (please see previous discussion regarding Pysh et al. 1999 in addressing the written description rejection). Applicants have disclosed sequences having sequence identities of 61%, 65%, and 100%, i.e., the low sequence identity and the high sequence identity which set up the boundary of the claimed genus, and have set guidance of generating sequences of similar structure and function, for example, the first paragraph at page 18. There is no need to disclose and test every sequence species that is more than 68% and less than 100% identical to SEQ ID NO: 4, and has also three conserved SCR domains similar to SEQ ID NO: 4, because one of ordinary skill in the art can easily generate sequences that have the desired sequence identity within the claimed range to SEQ ID NO: 4 through conserved amino acid substitutions or similar amino acid substitutions, for example, the substitutions listed in Table 3 or Table 4 of the specification, outside the conserved SCR domains, and they would have the similar function to G922.

Applicants note that they are not required to make and test every possible species within the claimed genus. In *Capon v. Eshhar*, the court noted that "[i]t is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention" *Capon v. Eshhar*, 418 F. 3d 1349, 1359 (Fed Cir. 2005). However, if one wishes to do so, methods for testing these sequences variants for greater tolerance to water deprivation is disclosed and routine. Applicants note that the fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation "must not be unduly extensive." Altas Powder Co., v. E.I. DuPont De Nemours & Co., 750 F. 2d 1569, 1576 (Fed. Cir. 1984). Given the disclosure of the conserved structure elements and related functional characteristics present in the exemplar sequences from diverse plant species, the detailed guidance of how to identify sequences of the disclosed structure and function through percent

identity, and the knowledge in the art at the time of filing, it would at most require routine experimentation to obtain other sequences encoding polypeptides having more than 60% sequence identity to SEQ ID NO: 4 and conferring enhanced water deprivation tolerance when overexpressed. Thus, Applicants believe that the full scope of currently claimed subject matter is enabled.

Accordingly, Applicant respectfully requests that the rejection of the claims under 35 USC 112, first paragraph, for lack of enablement, be withdrawn.

Item 11. Rejection under 35 USC 103 (a)

The Office action rejected claims 71-79 under 35 USC (a) based on the teachings of Benfey et al (WO97/41152) in further view of Benfey et al (U.S. Patent 6,411,270, filed 24 April 1997) and Pysh et al (1999, The Plant Journal 18(1): 111-119). This rejection has been respectfully traversed for the reason set forth below. Specific elements of the Office action are cited in bold face.

Firstly, the inventor of U.S. Patent 6,411,270 is Toshifumi, not Benfey, nor does the referred patent concerns DNA or protein sequences.

SEQ ID NO: 21 of Benfey is 68.2% identical to instant SEQ ID NO: 4 and comprises 63% of the first conserved domain of amino acids 134-199 of instant SEQ ID NO: 4. (page 11 of the Office action)

Applicants thank the Examiner for providing the sequence alignments and acknowledging that Benfey sequence comprises 63% of the first conserved domain of amino acids 134-199 of instant SEQ ID NO: 4. The present claim is limited to sequences that have a first conserved domain that is at least 68% of amino acids 134-199, therefore, the Benfey sequence falls out of the claimed scope.

Benfey had taught that the SRPa3 encoding polynucleotide was partial (1.231kb), Pysh had taught that the full length mRNA is approximately 1.8 Kb. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by Applicants.

In response, Applicants note that although Pysh did show that SCL3 was expressed in root by RNA blot analysis and estimated the band in the blot as 1.8 Kb, Pysh did not disclose the

complete sequence of SCL3 (syn. SRPa3). A band in a DNA gel can hardly be regarded as representing any specific structure of a full length DNA molecule. Pysh did not teach the presently claimed sequences. The only related sequence in Pysh's disclosure lacks the 157 amino acids of the instant SEQ ID NO: 4, the missing part includes the 24 amino acids that make up the first conserved SCR domain (please see the previous response regarding the partial sequence). Combining Pysh and Benfey would not cure the deficiency of lacking the structure of the full length sequence.

> **The fact that the prior art would have made the claimed invention for a different reason is addressed above.**
> **It is not invention to perceive that the product which others had discovered had qualities they failed to detect; and In re Wiseman, 596 F.2d 1019, 1023 (CCPA 1979) which states, rejecting the notion that " a structure suggested by the prior art, and hence, potentially in the possession of the public, is patentable… because it also possesses an inherent, but hitherto unknown, function which (patentees] claim to have discovered. This is not the law. A patent on such a structure would remove from public that which is in the public domain by virtue of its inclusion in, or obviousness from the prior art." (page 18, Office action)**

In response, transgenic plants claimed in the instant application not only comprise sequences with the predictable structural elements in terms of the conserved domains and overall protein structure by percent identity through BLAST, but also have greater tolerance to water deprivation compared to control plants. The MPEP requires that "Examiners must account for all claim limitations in their rejections by explaining how each limitation is disclosed or rendered obvious by the reference(s) applied. 'All words in a claim must be considered in judging the patentability of that claim against the prior art'" *In re Wilson*, 424 F. 2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970) MPEP 2143.03. The Office action did not take into account the functional limitation that is crucial for identifying the claimed genus. Benfey's prediction that SCR proteins have the abilities to confer thicker root does not render plants that over-express SCR proteins and have greater tolerance to water deficit obvious. 35 U.S.C. 103(a) demands consideration of "the subject matter sought to be patented.. as a whole" (MPEP 2141). When asserting a *prima facie* case of obviousness, "the burden falls on the Examiner to show.. that a person of ordinary skill in the art would have had reason to attempt to … carry out the claimed process, and would have had a reasonable expectation of success in doing so." *Pharmastem*

Therapeutics v. Viacell, Inc. 491 F.3d 1342, 1360 (Fed cir. 2007). The Office action failed to reason why water deprivation tolerance is obvious in view of the plants transformed with the partial sequence or the full length counterpart and having thicker root development.

Applicants respectfully remind the Examiner that it is not the transgenic plants transformed with the full length sequence of G922 that were claimed by the instant application, but rather a specific subset of those that have water deficit tolerance. Even if the complete sequence of G922 were obtainable before Applicants' disclosure, no trait of water deficit tolerance has ever been suggested for transgenic plants transformed with G922 polynucleotide by Benfey or Pysh. Please see MPEP 2144.08 (II): "The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. *In re Baird*, 16 F. 3d 380, 382, 29 USPQ2d 1550, 1552 (Fed Cir. 1994) ("the fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious." MPEP 2144.08 requires "Office personnel should ascertain the difference between the closest disclosed prior art species or subgenus of record and the claimed species or subgenus, … and compare it to the claimed species or subgenus to determine the differences, … make explicit findings on the similarities and differences between the closest disclosed prior art species or subgenus of record and the claimed species or subgenus including findings relating to similarity of structure, chemical properties and utilities." As we have seen with the evidence presented in Dr. Reuber's declaration submitted previously to the Office, the instantly claimed genus, i.e., plants overexpressing G922 (SEQ ID NO: 4) and having greater water deficit tolerance, do not have thicker root development; quite on the contrary, a lot of the overexpressors had less root development than control plants.

The Office action alleged that greater tolerance to water deficit is an inherent but unknown function of the transgenic plants expressing G922 from Benfey's disclosure. This is not correct. The Federal Circuit has ruled that inherency cannot be "established by probabilities or possibilities" and that, the mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson*, 49 USPQ2d 1949, 1951 (Fed. Cir. 1999). The court stated that the burden falls on the examiner to "provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic

necessarily flows from the teachings of the applied prior art." *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original). The Office action has not provided a factual basis or technical reasoning to support a finding of inherency based on Benfey or Pysh. Applicants' own experimental evidence demonstrated that greater tolerance to water deficit does not necessarily flow from overexpression of the claimed sequences. As shown in the declaration from by Dr. Ratcliffe (submitted on February 10, 2009): while both G3811 and G3810 (G922 orthologs) were observed to confer greater water deficit tolerance, eight of ten lines transformed with 35S::G3811 and seven of ten lines transformed with 35S:G3810 do not have greater water deficit tolerance. The declaration from Dr. Reuber, attached, also shows that similar to G3810 or G3811 overexpressors, not all transgenic plants overexpressing G922 displayed greater tolerance to water deficit: four lines did, but sixteen lines showed no discernible difference compared to control plants.

Regarding what constitutes inherency, please see *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004)("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention.") (emphasis added).

"The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted). (MPEP 2112(IV) (emphasis added).

Therefore, water deficit tolerance is not necessarily present, and thus not an inherent trait

or function of transgenic plants expressing SRPa3.

> **In re Kubin, 90 USPQ2d 1417, 1422 (Fed. Cir. 2009) which teaches that insofar as Deuel implies the obviousness inquiry cannot consider that the combination of the claim's constituent elements was "obvious to try," the Supreme court in KSR unambiguously discredited that holding. In the instant case, the prior art had taught a substantial portion of the SRPa3 encoding polynucleotide, and had taught that one of ordinary skill in the art could transform a plant with a polynucleotide that encode the SRPa3 polypepitde. At the time of Applicants invention it was routine to use a partial coding sequence to identify and isolate the complete coding sequence from an mRNA library. ...**
> **Given the general high level of skill in the instant art at the time of Applicants' invention, one of ordinary skill in the art would have had a reasonable expectation of success. (page 14 of Office action)**

In response, Applicants note that "obvious to try" in KSR applies to that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." KSR, 127 S. ct. at 1739. As stated above, having greater tolerance to water deficit tolerance is not predicable with plants transformed with G922 (SEQ ID NO: 3).

It is not obvious to try to make G922 transformants and test for water deprivation in view of Benfey even if the techniques and tools are available. Water deprivation tolerance is only one of the very large number of possible phenotypes that a plant could have and that were not suggested or tested by Benfey. Even the combination of Benfey and Pysh fails to cure the deficiency of lacking the functional limitation of conferring greater tolerance to water deprivation. Benfey prophetically disclosed that SRPa3-overexpressing plants have thicker roots. In view of Benfey's and Pysh's disclosure, if one of ordinary skill had introduced Benfey sequences into plants and tested for thicker roots, and if he, like Applicants, observed that none of the plants had thicker root and some of them had even less root development, he would have doubts on the accuracy of the Benfey disclosure, and he would not likely pursue any further use of these transgenic plants, including testing these plants for greater tolerance to water deficit. Thus, a person of ordinary skill in the art would not have tried to combine Benfey and Pysh to produce plants that have greater tolerance to water deficit by overexpressing G922, nor would he have a reasonable expectation of doing so in light of the combined teachings of the cited references only. The Office could not have found an expectation of success of producing G922-overexpressing transgenic plants that have greater tolerance to water deficit, without the Applicants' own disclosure in hand. The Supreme Court has "warn [ed] against 'temptation to

read into the prior art the teachings of the invention in issue' and instruct[ed] courts to 'guard against slipping into the use of hindsight.'" *KSR Int'l* v. *Teleflex Inc.,* 127 S.Ct 1742 (2007), quoting *Graham* v. *John Deere Co.,* 383 U.S. at 36. Therefore, the claimed invention is unobvious over Benfey and Pysh.

Accordingly, Applicants respectfully request the rejection under 35 U.S.C. §103(a) be withdrawn.

CONCLUSION

Applicants believe that no additional fee is due with this communication. However, if the USPTO determines that an additional fee is due, the Commissioner is hereby authorized to charge Mendel Biotechnology, Inc. Deposit Account No. 50-1025.

Respectfully submitted,
MENDEL BIOTECHNOLOGY, INC.

Date: February 5, 2010

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File: MBI-0058CIP.ROA11-9-09.doc

Attachments: GRAS domain of NCBI
Doerks 2002
Eisen, 1998
Reuber declaration

Exhibit A. Comparison of G922 and phylogenetically related sequences

The sequence identity was determined by BLASTP program using as defaults a wordlength (W) of 3, an expectation (E) of 10, and the BLOSUM62 scoring matrix.

```
>G3824 (Amino Acid Sequence) (gf=9)
          Length = 385

 Score =  541 bits (1394), Expect = e-155
 Identities = 275/394 (69%), Positives = 334/394 (84%), Gaps = 11/394 (2%)

G922 : 91  MQRIAAYFTEALANRILKSWPGLYKALNATQTRTNNVSEEIHVRRLFFEMFPILKVSYLL 150
          MQRIA+YFTEALA+RIL+SWPGLYKAL +T+     VSEEI VR++FFE+FP LKV++++
G3824: 1   MQRIASYFTEALADRILRSWPGLYKALRSTKLSV--VSEEILVRKMFFEIFPFLKVAFVV 58

G922 : 151 TNRAILEAMEGEKMVHVIDLDASEPAQWLALLQAFNSRPEGPPHLRITGVHHQKEVLEQM 210
          TN+AI+EAMEGEKMVH++DL+A+EP QW ALLQ  ++RPEGPPHLRITGVH QKEVL+QM
G3824: 59  TNQAIIEAMEGEKMVHIVDLNAAEPLQWRALLQDLSARPEGPPHLRITGVHQQKEVLDQM 118

G922 : 211 AHRLIEEAEKLDIPFQFNPVVSRLDCLNVEQLRVKTGEALAVSSVLQLHTFLASDDDLMR 270
          AH L +EAEKLDIPFQFN VVSRL+ L+VE+LRVKTGEALA+SS++QLHT LA D+D
G3824: 119 AHVLTQEAEKLDIPFQFNQVVSRLENLDVEKLRVKTGEALAISSIMQLHTLLAHDND--- 175

G922 : 271 KNCALRFQNNPSGVDLQRVLMMSHGSAAEARENDMSNNNGYSPSGDSASSLPLPSSGRT- 329
          K   L F+++ +GV+L R L+ +  +  E  E DM+N  G SPS D+ASS PL S+G T
G3824: 176 KKSPLPFKHS-NGVNLNRALV-NQNTLGEFLEKDMAN--GCSPSNDTASSSPLCSTGSTK 231

G922 : 330 -DSFLNAIWGLSPKVMVVTEQDSDHNGSTLMERLLESLYTYAALFDCLETKVPRTSQDRI 388
           DSFLNA+WGLSPKVMVVTEQD++HNG+TLMERL ESL+ YAALFDCLE+ +PRTS +R+
G3824: 232 MDSFLNALWGLSPKVMVVTEQDANHNGTTLMERLSESLHFYAALFDCLESTLPRTSLERL 291

G922 : 389 KVEKMLFGEEIKNIISCEGFERRERHEKLEKWSQRIDLAGFGNVPLSYYAMLQARRLLQG 448
          KVEKML GEEI+NII+CEG ER+ERHEKLEKW QR D +GFGNVPLSYYAMLQARRLLQ
G3824: 292 KVEKMLLGEEIRNIIACEGIERKERHEKLEKWFQRFDTSGFGNVPLSYYAMLQARRLLQS 351

G922 : 449 CGFDGYRIKEESGCAVICWQDRPLYSVSAWRCRK 482
             +GY+IKE++GC VICWQDRPL+SVS+WRCRK
G3824: 352 YSCEGYKIKEDNGCVVICWQDRPLFSVSSWRCRK 385



>G3813 (Amino Acid Sequence) (gf=9)
          Length = 442

 Score =  469 bits (1206), Expect = e-133
 Identities = 250/479 (52%), Positives = 321/479 (67%), Gaps = 39/479 (8%)

G922 : 4   MFQEDNGTSSVASSPLQVFSTMSLNRPTLLASSSPFHCLKDLKPEERGLYLIHLLLTCAN 63
          M Q++  +SSV SSPL  FS M L+ P   AS +P   +++L+ +ERGL LIHLLL CA
G3813: 1   MVQDEGSSSSVTSSPLHNFSNMPLH-PAAAASPTPPWMVRELRSDERGLCLIHLLLNCAA 59

G922 : 64  HVASGSLQNANAALEQLSHLASPDGDTMQRIAAYFTEALANRILKSWPGLYKALNATQTR 123
            A+G L  ANAALE ++ LA+PDGD MQR+AA F EALA R L++WPGL +AL   +
G3813: 60  AAAAGRLDAANAALEHIASLAAPDGDAMQRVAAAFAEALARRALRAWPGLCRALLLPRA- 118

G922 : 124 TNNVSEEIHVRRLFFEMFPILKVSYLLTNRAILEAMEGEKMVHVIDLDASEPAQWLALLQ 183
          +   +E    RR F ++ P L+++    N++ILEAME EK+VHVIDL  ++  QWL LL
G3813: 119 SPTPAEVAAARRHFLDLCPFLRLAGAAANQSILEAMESEKIVHVIDLGGADATQWLELLH 178
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G922 : 184 AFNSRPEGPPHLRITGVHHQKEVLEQMAHRLIEEAEKLDIPFQFNPVVSRLDCLNVEQLR 243
              +RPEGPPHLR+T VH  KE+L Q A  L +EAE+LD+PFQFNPVVSRLD L+VE LR
G3813: 179 LLAARPEGPPHLRLTSVHEHKELLTQTAMALTKEAERLDVPFQFNPVVSRLDALDVESLR 238

G922 : 244 VKTGEALAVSSVLQLHTFLASDDDLMRKNCALRFQNNPSGVDLQRVLMMSHGSAAEAREN 303
           VKTGEALA+ S LQLH  LASDDD                                + A   +
G3813: 239 VKTGEALAICSSLQLHCLLASDDDA-------------------------AAVAGGDKE 272

G922 : 304 DMSNNNGYSPSGDSASSLPLPSSGRTDSFLNAIWGLSPKVMVVTEQDSDHNGSTLMERLL 363
             S  +G S           PS+ R D+FL A+WGLSPKVMVV EQ++ HN + L ER +
G3813: 273 RRSPESGLS-----------PSTSRADAFLGALWGLSPKVMVVAEQEASHNAAGLTERFV 321

G922 : 364 ESLYTYAALFDCLETKVPRTSQDRIKVEKMLFGEEIKNIISCEGFERRERHEKLEKWSQR 423
           E+L  YAALFDCLE    R S +R +VE+ L GEEIKNI++C+G ERRERHE+LE+W++R
G3813: 322 EALNYYAALFDCLEVGAARGSVERARVERWLLGEEIKNIVACDGGERRERHERLERWARR 381

G922 : 424 IDLAGFGNVPLSYYAMLQARRLLQGCGFDGYRIKEESGCAVICWQDRPLYSVSAWRCRK 482
           ++ AGFG VPLSYYA+LQARR+ QG G DG++++EE G   +CWQDR L+SVSAWR R+
G3813: 382 LEGAGFGRVPLSYYALLQARRVAQGLGCDGFKVREEKGNFFLCWQDRALFSVSAWRGRR 440


>G3814 (Amino Acid Sequence) (gf=9)
         Length = 517

 Score =  339 bits (869), Expect = 2e-94
 Identities = 209/502 (41%), Positives = 295/502 (58%), Gaps = 47/502 (9%)

G922 : 4   MFQEDNGTSSVASSPLQVFSTMSLNRPTLLASSSPFHCLKDLKPEERGLYLIHLLLTCAN 63
           MFQ+D  +S+ +S    V+S           S S    +++L  +++ + LI LL  CA
G3814: 1   MFQDDMLSSATSSPASSVYSPSP--------SPSNGSWVQELSHDQQSVRLIGLLYQCAA 52

G922 : 64  HVASGSLQNANAALEQLSHLASPDGD-TMQRIAAYFTEALANRILKSWPGLYKALNATQT 122
            V++GS   AN  LE ++ LAS D    +QR+AA F +ALA ++L    GL +AL ++
G3814: 53  EVSAGSFDRANLCLEHITQLASLDAPHALQRLAAVFADALARKLLNLILGLSRALLSSAN 112

G922 : 123 RTNNVSEEIHV----RRLFFEMFPILKVSYLLTNRAILEAMEGEKMVHVIDLD--ASEPA 176
                S + H+    RR  F++ P LK++YL TN AILEAMEGE+ VHV+D    A+ P
G3814: 113 -----SADAHLVPVARRHMFDVLPFLKLAYLTTNHAILEAMEGERFVHVVDFSGPAANPV 167

G922 : 177 QWLALLQAFNSRPEGPPHLRITGVHHQKEVLEQMAHRLIEEAEKLDIPFQFNPVVSRLDC 236
           QW+AL  AF  R EGPPHLRIT VH  KE L  MA  L +EAE  DI FQFN V ++LD
G3814: 168 QWIALFHAFRGRREGPPHLRITAVHDSKEFLANMAAVLSKEAEAFDIAFQFNAVEAKLDE 227

G922 : 237 LNVEQLR----VKTGEALAVSSVLQLHTFLASDDDLMRKNCALRFQNNPSGVDLQRVLMM 292
           ++ + LR    V++GEALAVS VLQLH  LA DD   R++ A           +Q +
G3814: 228 MDFDALRHDLGVRSGEALAVSVVLQLHRLLAVDDG--RRHAAAGCL-----TPVQIIARS 280

G922 : 293 SHGSAAEARENDMSNNNGYSPSGDSASSL------------PLPSSGRTDSFLNAIWGLS 340
           S  S  E  E +++     SP     SSL            P  S+ +  SFL+A+  LS
G3814: 281 SPRSFGELLERELNTRLQLSPDASVVSSLSPHSPAAATAAHPTTSTPKLGSFLSAVRSLS 340

G922 : 341 PKVMVVTEQDSDHNGSTLMERLLESLYTYAALFDCLETKVPRTSQDRIKVEKMLFGEEIK 400
           PK+MV+TEQ+++HNG    ER  E+L  YA+LFDCL+ +    + +R +VE++L GEEI+
G3814: 341 PKIMVMTEQEANHNGGAFQERFDEALNYYASLFDCLQ-RSAAAAAERARVERVLLGEEIR 399

G922 : 401 NIISCEGFERRERHEKLEKWSQRIDLAGFGNVPLSYYAMLQARRLLQGCGFDG-YRIKEE 459
            +++CEG ER ERHE+  +W+ R++ AG   V LSY   ++AR+LLQ CG+ G Y ++ +
G3814: 400 GVVACEGAERVERHERARQWAARMEAAGMERVGLSYSGAMEARKLLQSCGWAGPYEVRHD 459
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G922 : 460 SG--CAVICWQDRPLYSVSAWR 479
           +G      CW  RPLY+V+AWR
G3814: 460 AGGHGFFFCWHKRPLYAVTAWR 481
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>G3827 (Amino Acid Sequence) (gf=9)
Length = 422

Score = 176 bits (446), Expect = 2e-45
Identities = 91/160 (56%), Positives = 115/160 (71%), Gaps = 8/160 (5%)

```
G922 : 324 PSSGRTDSF-LNAIWGLSPKVMVVTEQDSDHNGSTLMERLLESLYTYAALFDCLETKVPR 382
           P   R D+  + ++ GLS KVMVVTEQ+  HN + L ER +E+L  YAALFDCLE    R
G3827: 217 PVVSRLDALDVESLRGLSLKVMVVTEQEVSHNAAGLTERFVEALNYYAALFDCLEVGGAR 276

G922 : 383 TSQDRIKVEKMLFGEEIKNIISCEGFERRERHEKLEKWSQRIDLAGFGNVPLSYYAMLQA 442
            S +R +VE+ L GEEIKNI++C+G ERRERHE+LE        AGFG VPLSYYA+LQA
G3827: 277 GSVERTRVERWLLGEEIKNIVACDGGERRERHERLEG-------AGFGRVPLSYYALLQA 329

G922 : 443 RRLLQGCGFDGYRIKEESGCAVICWQDRPLYSVSAWRCRK 482
           RR+ QG G DG+++EE G   +CWQDR L+SVSAWR R+
G3827: 330 RRVAQGLGCDGFKVREEKGNFFLCWQDRALFSVSAWRGRR 369
```